

Appl. No. 10/061,128
 Amdt. dated October 29, 2003
 Reply to Office Action of November 21, 2003

Amendments to the Specification:

Please replace the paragraph starting at page 78, line 2 with the following amended paragraph:

Melting points were determined on a Mel-temp II laboratory device and are uncorrected. Nuclear magnetic resonance spectra were recorded on a Bruker 250 and AMX400 400 MHz spectrometers with tetramethylsilane as the internal reference; chemical shifts (δ) are reported in parts per million (ppm), and the signals are described as s (singlet), d (doublet), t (triplet), q (quartet), br s (broad singlet), dd (doublet of doublet), and m (multiplet). UV spectra were obtained on a beckman DU 650 spectrophotometer. Optical rotations were measured on a Jasco DIP-370 Digital Polarimeter. Mass spectra were measured on a Micromass Inc. Autospec High Resolution double focussing sector (EBE) MS spectrometers. Infrared spectra were recorded on a Nicolet 510 FT-IR spectrometer. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA. All reactions were monitored using thin layer chromatography on Analtech, 200 mm silica gel GF plates. Dry 1,2-dichloroethane, dichloromethane, and acetonitrile were obtained by distillation from CaH_2 prior to use. Dry THF was obtained by distillation from Na and benzophenone when the solution became purple.

Please replace the paragraph starting at page 78, line 15 with the following amended paragraph:

L-(S)-Glyceraldehyde acetonide (302). A solution of ~~L-gulonic- γ -lactone~~ L-gulonic- γ -lactone (175 g, 0.98 mol) in DMF (1 L) was cooled to ~~0-5~~ 0 °C and *p*-toluenesulfonic acid (1.1 g, 5.65 mmol) was added portionwise with stirring. To the resulting solution, 2-methoxypropene (87.7 g, 0.92 mol) was added dropwise through a dropping funnel at ~~0-5~~ 0 °C. The reaction mixture was warmed up to room temperature and further stirred for 24 h. After the completion of the reaction, sodium carbonate (124 g) was added and the resulting suspension was vigorously stirred for 3 hours. It is then filtered over glass filter and the filtrate is evaporated under vacuum. To the yellow residue, toluene (170 mL) is added whereupon crystallization occurred. The solid was filtered by suction, washed with hexanes/ethanol (9:1; 1 L), and dried to give yellowish solid **301** (99.1 g, 65 %).

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Please replace the paragraph starting at page 79, line 3 with the following amended paragraph:

To a stirred suspension of 5,6-*O*-isopropylidene-L-gulono-1,4-lactone (70.0 g, 0.32 mol) in water (270 mL), sodium metaperiodate (123 g, 0.58 mol) was added portionwise at $0 \pm 0^\circ\text{C}$ over 30 min maintaining pH 5.5 (adjusted by addition of 2 N NaOH). The suspension was stirred at room temperature for 2 hours, then saturated with sodium chloride and filtered. The pH of the filtrate was adjusted to 6.5-7.0 and extracted with dichloromethane (5 times 200 mL) and ethyl acetate (5 times 300 mL). The combined organic layer were dried with anhydrous magnesium sulfate, filtered and concentrated under reduced pressure ($< 20 \pm 0^\circ\text{C}$) ($< 20^\circ\text{C}$). And then the resulting residue was distilled to give **302** (23.2 g, 69 %) as a colorless oil; b.p. 49-51 $\pm 0^\circ\text{C}$ / 16 Torr. $[\alpha]_{\text{D}}^{25}$ ~~$[\alpha]_{\text{D}}^{25}$~~ $[\alpha]_{\text{D}}^{25}$ -66.4 (c 6.3, benzene).

Please replace the paragraph starting at page 79, line 12 with the following amended paragraph:

(*E*)/(*Z*)-Ethyl-3-[(*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2-fluoroacrylate (*E*-303 and *Z*-303). A solution of triethyl 2-fluorophosphonoacetate (39.2 g, 162 mmol) in THF (70 mL) was cooled to $-78 \pm 0^\circ\text{C}$ and a solution of sodium bis(trimethylsilyl)amide (1.0 M solution in THF, 162 mL, 162 mmol) was added dropwise. The mixture was kept for 30 min at $-78 \pm 0^\circ\text{C}$, then a solution of **303** (19.14 g, 147 mmol) in THF (70 mL) was added. After being stirred for 1 h at $-78 \pm 0^\circ\text{C}$, the reaction mixture was treated with aqueous NH_4Cl and extracted with ether. The ether phase was washed with saturated NaCl, dried over MgSO_4 , filtered and evaporated. The residue was chromatographed on silica gel to give *E*-303 and *Z*-303 (9:1 by ^1H NMR) as a pale yellowish oil (34.6 g, 97.9 %). ^1H NMR (CDCl_3) δ 1.34, 1.36 (2t, $J = 8$ Hz, $-\text{CH}_2\text{CH}_3$), 1.40, 1.45 (2s, $-\text{CH}_3$), 3.69 (m, H_a -5), 4.28 (m, H_b -5, $-\text{CH}_2\text{CH}_3$), 5.02 (m, H-4), 5.40 (m, H-4), 6.02 (dd, $J = 8, 20$ Hz, H-3), 6.18 (dd, $J = 8, 32$ Hz, H-3).

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Please replace the paragraph starting at page 80, line 1 with the following amended paragraph:

(R)-(+)-4-[(*tert*-Butyldimethylsilyloxy)methyl]-2-fluoro-2-buten-4-olide (307). A solution of *E*-303 and *Z*-303 (19.62 g, 89.89 mmol) in 110 mL of anhydrous EtOH was treated with 30 mL of conc. HCl and stirred at room temperature for 2 hr. The solvent was removed in vacuo and the residue was coevaporated with Toluene (3*300 mL) to give the lactone 304 and uncyclized ester 305. The resulting yellowish syrup was used for next reaction without further purification. *t*-Butyldimethylsilyl chloride (27.1 g, 180 mmol) was added to a mixture of 304, 305 and imidazole (12.3 g, 180 mmol) in CH₂Cl₂ (250 mL) and the reaction mixture was stirred for 4-h at room temperature. The resulting mixture was washed with water, dried (MgSO₄), filtered and concentrated to dryness. The residue was isolated by silica gel column chromatography using 4% EtOAc-hexanes as an eluent to give 307 (28.0g, 70.2% from compound 302) as a white crystalline solid. mp 48-50 °C; $[\alpha]_D^{28} +105.3$ (c 1.60, CHCl₃); ¹H NMR (CDCl₃) δ 0.07, 0.08 (2s, 2 x CH₃), 0.88 (s, ^tBu), 3.88 (m, 2H, H-5), 5.01 (m, 1H, H-4), 6.73 (ps t, 1H, J = 4 Hz); Anal. Calcd for C₁₀H₁₉FO₃Si: C, 53.63; H, 7.77. Found: C, 53.70; H, 7.75.

Please replace the paragraph starting at page 80, line 14 with the following amended paragraph:

1-Acetyl-4-[(*tert*-butyldimethylsilyloxy)methyl]-2-fluoro-2-buten-4-olide (309). Lactone 307 (20.58 g, 83.54 mmol) was dissolved in 200 mL of CH₂Cl₂ under nitrogen atmosphere, then the mixture was cooled to -78 °C and 1.0 M solution of DIBAL-H in CH₂Cl₂ (125 mL) was added. The resulting mixture was stirred for 2 hours at -78 °C. The cold mixture was treated with dilute nitric acid, washed with water, and dried (Na₂SO₄). Evaporation of the solvent gave anomers of 308 as a pale yellow oil (16.6 g, crude yield 80 %), which was used for the next step without further purification.

Please replace the paragraph starting at page 80, line 21 with the following amended paragraph:

Ac₂O (25 mL, 0.27 mol) was added to a solution of 308 and pyridine (22 mL, 0.27 mol) in CH₂Cl₂ (200 mL) at 0 °C and the resulting mixture was stirred for 16 hours. The reaction mixture was washed

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with dilute HCl, saturated NaHCO₃ solution, and brine. The combined organic layer was dried, filtered, and concentrated to dryness. The residue was column chromatographed (6.5 % EtOAc/hexanes) to give **309** (12.6 g, 65 %) as a colorless oil.

Please replace the paragraph starting at page 81, line 4 with the following amended paragraph:

A mixture of uracil (420 mg, 3.75 mmol), hexamethyldisilazane (15 mL) and ammonium sulfate (20 mg) was refluxed for 3 hours under nitrogen. The clear solution obtained was concentrated to dryness *in vacuo*. TMSOTf (0.7 mL, 3.14 mmol) were added to the solution of sugar **309** (728 mg, 2.50 mmol) and the silylated base in dry DCE (20 mL) at 0 °C. The reaction mixture was stirred for 2 hours under nitrogen, poured into a cooled sat. NaHCO₃ solution (30 mL) and stirred for 15 min. The resulting mixture was washed, dried (Na₂SO₄), filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography (3 % MeOH/CHCl₃) to give **310** (0.960 g, 2.73 mmol, 73 %) as an inseparable anomeric mixture, which was used in the next step without separation.

Please replace the paragraph starting at page 81, line 15 with the following amended paragraph:

UV (CHCl₃) ϵ_{\max} λ_{\max} 257.5 nm.; Anal. (C₁₅H₂₃FN₂O₄Si) C, H, N.

Please replace the paragraph starting at page 81, line 18 with the following amended paragraph:

Silylated thymine (242 mg, 1.92 mmol), **307** (500 mg, 1.72 mmol), and TMSOTf (0.5 mL, 2.25 mmol) were reacted for 2 h to give a mixture of **311**, which was purified by silica gel column chromatography (3 % MeOH/CHCl₃) as an inseparable anomeric mixture (0.392 g, 1.10 mmol, 64 %). UV (CHCl₃) ϵ_{\max} λ_{\max} 262.0 nm. Anal. (C₁₆H₂₅FN₂O₄Si) C, H, N.

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Please replace the paragraph starting at page 82, line 1 with the following amended paragraph:

Silylated *N*⁶-benzoyl cytosine (790 mg, 3.67 mmol), 307 (470 mg, 1.62 mmol), and TMSOTf (0.5 mL, 2.25 mmol) were reacted for 2 h to give mixtures of 312 and 313, which were purified by silica gel column (30 % EtOAc/hexane) to afford β anomer 312 (0.34 g, 0.76 mmol, 47.1 %) as a white solid and α anomer 313 chromatography (0.23 g, 0.52 mmol, 31.8 %) as a white solid. 312: UV (CHCl₃) ϵ_{max} λ_{max} 260.5 nm; Anal. (C₂₂H₂₈FN₃O₄Si) C, H, N.; 313: UV (CHCl₃) ϵ_{max} λ_{max} 260.5 nm.; Anal. (C₂₂H₂₈FN₃O₄Si) C, H, N.

Please replace the paragraph starting at page 82, line 10 with the following amended paragraph:

Silylated 5-fluoro-cytosine (300 mg, 2.32 mmol), 309 (360 mg, 1.24 mmol), and TMSOTf (0.4 mL, 1.86 mmol) were reacted for 2 h to give a mixture of 314 and 315, which was purified by silica gel column chromatography (3 % MeOH/CH₂Cl₂) to afford β anomer 314 as a white solid (168 mg, 37.8 %) and α anomer 315 (121 mg, 27.1 %) as a white solid. 314: UV (MeOH) ϵ_{max} λ_{max} 281.5 nm; 315: UV (MeOH) ϵ_{max} λ_{max} 281.5 nm.

Please replace the paragraph starting at page 82, line 15 with the following amended paragraph:

~~1-(2,3-Dideoxy-2-fluoro-(α,β)-L-gycero-pent-2-eno-furanosyl)uracil~~

1-(2,3-Dideoxy-2-fluoro-(α,β)-L-gycero-pent-2-eno-furanosyl)uracil (316 and 317).

Tetra-*n*-butylammonium fluoride (0.6 mL, 0.6 mmol) was added to a mixture of 310 (177 mg, 0.52 mmol) in THF (15 mL) and the reaction mixture was stirred at room temperature for 15 min. The solvent was removed and the residue was purified by silica gel column chromatography (2 % MeOH/CHCl₃) to give β anomer 316 (52.8 mg, 0.23 mmol, 44.5 %) and α anomer 317 (35.1 mg, 0.15 mmol, 29.6 %).

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Please replace the paragraph starting at page 82, line 21 with the following amended paragraph:

316: UV (H₂O) ϵ_{\max} λ_{\max} 261.0 nm (pH 7); Anal. (C₉H₉FN₂O₄·0.3H₂O) C, H, N. 317: UV (H₂O) ϵ_{\max} λ_{\max} 261.0 nm (pH 7); Anal. (C₉H₉FN₂O₄·0.2H₂O) C, H, N.

Please replace the paragraph starting at page 82, line 23 with the following amended paragraph:

~~1-(2,3-Dideoxy-2-fluoro- α,β -L-glycero-pent-2-eno-furanosyl)thymine~~

1-(2,3-Dideoxy-2-fluoro-(α,β)-L-glycero-pent-2-eno-furanosyl)thymine (318 and 319).

Tetra-*n*-butylammonium fluoride (0.8 mL, 0.8 mmol) was added to a mixture of 311 (240 mg, 0.67 mmol) in THF (10 mL) at 0 °C and the reaction mixture was stirred at room temperature at rt for 15 min. The solvent was removed and the residue was purified by silica gel column chromatography (40 % THF/cyclohexane) to give β anomer 318 (66.5 mg, 0.28 mmol, 41 %) and α anomer 319 (52.8 mg, 0.23 mmol, 26 %).

Please replace the paragraph starting at page 83, line 4 with the following amended paragraph:

318: UV (H₂O) ϵ_{\max} λ_{\max} 265.5 nm (pH 7); Anal. (C₁₀H₁₁FN₂O₄·0.4H₂O) C, H, N. 319: UV (H₂O) ϵ_{\max} λ_{\max} 266.0 nm (pH 7); Anal. (C₉H₉FN₂O₄·0.3H₂O) C, H, N.

Please replace the paragraph starting at page 83, line 6 with the following amended paragraph:

~~N⁶-Benzoyl-1-(2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl)cytosine (320).~~

N⁶-Benzoyl-1-(2,3-dideoxy-2-fluoro- β -L-glycero-pent-2-enofuranosyl)cytosine (320).

Tetra-*n*-butylammonium fluoride (1M in THF) (1 mL, 1 mmol) was added to a solution of the α anomer β anomer 312 (280 mg, 0.63 mmol) in THF (10 mL) and the reaction was allowed to stir at room temperature for 1h. The reaction mixture was concentrated under the reduced pressure and the residue

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was purified by flash silica gel column using 2.5 % MeOH/CHCl₃ to give **320** (218 mg, 0.66 mmol, 75 %) as a white solid.

Please replace the paragraph starting at page 83, line 12 with the following amended paragraph:

UV (MeOH) ϵ_{\max} λ_{\max} 260.5 nm. Anal. (C₁₆H₁₄FN₃O₄) C, H, N.

Please replace the paragraph starting at page 83, line 13 with the following amended paragraph:

~~N⁶-Benzoyl-1-(2,3-dideoxy-2-fluoro- β -L-glycero-pent-2-enofuranosyl)cytosine (321).~~

N⁶-Benzoyl-1-(2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl)cytosine (321).

Tetra-*n*-butylammonium fluoride (1M in THF) (1 mL, 1 mmol) was added to a solution of the β -anomer α anomer 313 (280 mg, 0.63 mmol) in THF (10 mL) and the reaction was allowed to stir at room temperature for 1h. The reaction mixture was concentrated under the reduced pressure and the residue was purified by silica gel column chromatography using 2.5 % MeOH/CHCl₃ to give **321** (145.8 mg, 0.44 mmol, 69 %) as a white solid.

Please replace the paragraph starting at page 83, line 19 with the following amended paragraph:

UV (MeOH) ϵ_{\max} λ_{\max} 260.5 nm. Anal. (C₁₆H₁₄FN₃O₄ .0.3H₂O) C, H, N.

Please replace the paragraph starting at page 83, line 20 with the following amended paragraph:

~~1-(2,3-dideoxy-2-fluoro- β -L-glycero-pent-2-enofuranosyl)cytosine (322).~~

1-(2,3-dideoxy-2-fluoro- β -L-glycero-pent-2-enofuranosyl)cytosine (322). A solution of the β -anomer

β anomer (67.60 mg, 0.204 mmol) in MeOH (5 mL) was treated with NH₃/MeOH (10 mL saturated solution) and the reaction mixture was allowed to stir at room temperature until the disappearance of starting material was observed (10 h). The reaction mixture was concentrated under reduced pressure

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and the residue was purified by preparative TLC using 12 % MeOH/CH₂Cl₂ as an eluent. The material obtained from the plate gave 322 (43 mg, 93.1 %) as a solid on trituration with hexanes and diethylether.

Please replace the paragraph starting at page 84, line 4 with the following amended paragraph:

UV (H₂O) ϵ_{\max} λ_{\max} 266.5 nm (pH 7); Anal. (C₉H₁₀FN₃O₃·0.4H₂O) C, H, N...

Please replace the paragraph starting at page 84, line 5 with the following amended paragraph:

~~1-(2,3-dideoxy-2-fluoro- α -L-gycero-pent-2-enofuranosyl)cytosine.~~

1-(2,3-dideoxy-2-fluoro- α -L-gycero-pent-2-enofuranosyl)cytosine (323). A solution of the ~~α anomer~~ α anomer (65.90 mg, 0.199 mmol) in MeOH (5 mL) was treated with NH₃/MeOH (10 mL saturated solution) and the reaction mixture was allowed to stir at room temperature until the disappearance of starting material was observed (16 h). The reaction mixture was concentrated under reduced pressure and the residue was purified by preparative TLC using 12 % MeOH/CH₂Cl₂ as an eluent. The material obtained from the plate gave 322 (42.5 mg, 94.5 %) as a solid on trituration with hexanes and diethylether.

Please replace the paragraph starting at page 84, line 12 with the following amended paragraph:

UV (H₂O) ϵ_{\max} λ_{\max} 276.0 nm (pH 2), 267.0 nm (pH 7); Anal. (C₉H₁₀FN₃O₃) C, H, N.

Please replace the paragraph starting at page 84, line 13 with the following amended paragraph:

~~5-Fluoro-1-(2,3-dideoxy-2-fluoro- α -L-gycero-pent-2-enofuranosyl)cytosine~~

5-Fluoro-1-(2,3-dideoxy-2-fluoro- β -L-gycero-pent-2-enofuranosyl)cytosine (324).

Please replace the paragraph starting at page 84, line 14 with the following amended paragraph:

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Tetra-*n*-butylammonium fluoride (1M in THF) was added to a solution of the ~~α -anomer~~ β anomer 314 in acetonitrile and the reaction was allowed to stir at room temperature for 1h. The reaction mixture was concentrated under the reduced pressure and the residue was purified by flash silica gel column using 12 % MeOH/CHCl₃ to give 324.

Please replace the paragraph starting at page 84, line 19 with the following amended paragraph:

~~5-Fluoro-1-(2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl)cytosine~~
5-Fluoro-1-(2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl)cytosine (325).

Please replace the paragraph starting at page 84, line 20 with the following amended paragraph:

Tetra-*n*-butylammonium fluoride (1M in THF) was added to a solution of the ~~α -anomer~~ β anomer 315 in acetonitrile and the reaction was allowed to stir at room temperature for 1h. The reaction mixture was concentrated under the reduced pressure and the residue was purified by flash silica gel column using 12 % MeOH/CHCl₃ to give 325.

Please replace the paragraph starting at page 85, line 14 with the following amended paragraph:

326: UV (MeOH) ϵ_{\max} λ_{\max} 265.0 nm; Anal. (C₁₆H₂₂ClFN₄O₂ Si) C, H, N.

Please replace the paragraph starting at page 85, line 15 with the following amended paragraph:

~~6-Chloro-2-fluoro-9-[5-O-(*tert*-butyldimethylsilyl)-2,3-dideoxy-2-fluoro-
 (α,β -L-glycero-pent-2-enofuranosyl)]purine~~
6-Chloro-2-fluoro-9-[5-O-(*tert*-butyldimethylsilyl)-2,3-dideoxy-2-fluoro-
 (α,β)-L-glycero-pent-2-enofuranosyl]purine (327 and 328).

Please replace the paragraph starting at page 85, line 17 with the following amended paragraph:

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A mixture of silylated 2-fluoro-6-chloropurine [prepared from 1.170 g (6.78 mmol) of 2-fluoro-6-chloropurine and dry DCE(40 mL) was stirred for 16 h at room temperature. After work-up similar to that of 326, purification by silica gel column chromatography (12 % EtOAc/hexanes) gave β -anomer 327 (685 mg, 1.70 mmol, 30.0 %) as a white foam and α -anomer 328 (502 mg, 1.25 mmol, 22.1 %) as an yellowish syrup.

Please replace the paragraph starting at page 85, line 22 with the following amended paragraph:

327: UV (MeOH) ϵ_{\max} λ_{\max} 268.5 nm. Anal. (C₁₆H₂₁F₂ClN₄O₂Si) C, H, N., 328: UV (MeOH) ϵ_{\max} λ_{\max} 269.0 nm. Anal. (C₁₆H₂₁F₂ClN₄O₂Si) C, H, N.

Please replace the paragraph starting at page 86, line 1 with the following amended paragraph:

~~6-Chloro-9-(2,3-dideoxy-2-fluoro-(β)-L-gycero-pent-2-enofuranosyl)purine~~

6-Chloro-9-(2,3-dideoxy-2-fluoro-(α , β)-L-gycero-pent-2-enofuranosyl)purine (329 and 330). A solution of 326 (1.2 g, 3.12 mmol) in dry CH₃CN (20 mL) was treated with TBAF (1 M solution in THF) (3.2 mL, 3.2 mmol) and stirred for 1 h. After evaporation of solvent, the dryness was purified by column chromatography (3 % MeOH/CHCl₃) to obtain β -anomer 329 (296 mg, 35 %) as a white solid and α -anomer 330 (380 mg, 45 %) as a foam.

Please replace the paragraph starting at page 86, line 6 with the following amended paragraph:

329: UV (MeOH) ϵ_{\max} λ_{\max} 265.0 nm.; 330: UV (MeOH) ϵ_{\max} λ_{\max} 265.0 nm.

Please replace the paragraph starting at page 86, line 8 with the following amended paragraph:

~~6-Amino-2-fluoro-9-[5-O-(tert-butylidimethylsilyl)-2,3-dideoxy-2-fluoro- β -L-gycero-pent-2~~

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~~-enofuranosyl]purine~~

~~6-Amino-2-fluoro-9-[5-O-(tert-butyldimethylsilyl)-2,3-dideoxy-2-fluoro- β -L-gycero-pent-2-
 -enofuranosyl]purine (331) and~~

Please replace the paragraph starting at page 86, line 10 with the following amended paragraph:

~~6-Chloro-2-amino-9-[5-O-(tert-butyldimethylsilyl)-2,3-dideoxy-2-fluoro- β -L-gycero-pent-2-
 -enofuranosyl]purine~~

6-Chloro-2-amino-9-[5-O-(tert-butyldimethylsilyl)-2,3-dideoxy-2-fluoro- β -L-gycero-pent-2-enofur
 anosyl]purine (332)

Please replace the paragraph starting at page 86, line 12 with the following amended paragraph:

Dry ammonia was bubbled into a stirred solution of **327** (420 mg, 1.04 mmol) in dry DME (35 mL) at room temperature overnight. The salts were removed by filtration and the filtrate was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (25 % EtOAc/hexanes) to give two compounds, **331** (114 mg, 0.30 mmol) as a white solid and **332** (164 mg, 0.41 mmol) as a white solid.

Please replace the paragraph starting at page 86, line 17 with the following amended paragraph:

331:UV (MeOH) ϵ_{\max} λ_{\max} 268.5 nm. Anal. (C₁₆H₂₃F₂N₅O₂ Si 0.2Acetone) C, H, N, **332**:UV (MeOH) ϵ_{\max} λ_{\max} 307.5 nm. Anal. (C₁₆H₂₃FN₅O₂ ClSi) C, H, N, Cl.

Please replace the paragraph starting at page 86, line 20 with the following amended paragraph:

~~6-Amino-2-fluoro-9-[5-O-(tert-butyldimethylsilyl)-2,3-dideoxy-2-fluoro- β -L-gycero-pent-2-enofura
 nosyl]purine~~

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6-Amino-2-fluoro-9-[5-O-(tert-butyldimethylsilyl)-2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl]purine (333) and

Please replace the paragraph starting at page 87, line 1 with the following amended paragraph:

~~6-Chloro-2-amino-9-[5-O-(tert-butyldimethylsilyl)-2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl]purine~~

6-Chloro-2-amino-9-[5-O-(tert-butyldimethylsilyl)-2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl]purine (334) .

Please replace the paragraph starting at page 87, line 9 with the following amended paragraph:

333: UV (MeOH) ϵ_{\max} λ_{\max} 269.0 nm. Anal. (C₁₆H₂₃F₂N₅O₂ Si 0.3Acetone) C, H, N, 334: UV (MeOH) ϵ_{\max} λ_{\max} 309.5 nm. Anal. (C₁₆H₂₃F ClN₅O₂ Si) C, H, N.

Please replace the paragraph starting at page 87, line 11 with the following amended paragraph:

~~9-(2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl)adenine~~

9-(2,3-dideoxy-2-fluoro- β -L-glycero-pent-2-enofuranosyl)adenine (335). A solution of 329 (100 mg, 0.369 mmol) and saturated NH₃/MeOH (50 mL) was heated at 90 \pm $^{\circ}$ C in a steel bomb for 24 h. After cooling to room temperature, the solvent was removed under reduced pressure and the residual syrup was purified by column chromatography using 6 % MeOH/CHCl₃ as an eluent to give 335 (70 mg, 75 %) as a white solid. 335: UV (H₂O) ϵ_{\max} λ_{\max} 258 nm (ϵ 18,800) (pH 2), 258.5 nm (ϵ 18,800) (pH 7), 258.5 nm (ϵ 19,100) (pH 11). Anal. (C₁₀H₁₀FN₅O₂ .0.2H₂O) C, H, N.

Please replace the paragraph starting at page 87, line 18 with the following amended paragraph:

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~~9-(2,3-dideoxy-2-fluoro- β -L-glycero-pent-2-enofuranosyl)adenine~~

9-(2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl)adenine (336). A solution of 330 (99 mg, 0.366 mmol) and saturated NH_3/MeOH (50 mL) was heated at $90 \pm 5^\circ\text{C}$ in a steel bomb for 24 h. After cooling to room temperature, the solvent was removed under reduced pressure and the residual syrup was purified by column chromatography using 6 % $\text{MeOH}/\text{CHCl}_3$ as an eluent to give 336 (72 mg, 78 %) as a white solid.

Please replace the paragraph starting at page 88, line 1 with the following amended paragraph:

336: UV (H_2O) ϵ_{max} λ_{max} 258 nm ~~(ϵ 21,100)~~ (ϵ 21,100) (pH 2), 259 nm ~~(ϵ 21,500)~~ (ϵ 21,500) (pH 7), 259 nm ~~(ϵ 22,600)~~ (ϵ 22,600) (pH 11). Anal. ($\text{C}_{10}\text{H}_{10}\text{FN}_5\text{O}_2 \cdot 0.3\text{MeOH}$) C, H, N.

Please replace the paragraph starting at page 88, line 3 with the following amended paragraph:

~~9-(2,3-dideoxy-2-fluoro- β -L-glycero-pent-2-enofuranosyl)hypoxanthine~~

9-(2,3-dideoxy-2-fluoro- β -L-glycero-pent-2-enofuranosyl)hypoxanthine (337). A mixture of 329 (100 mg, 0.369 mmol), NaOMe (0.5 M solution in MeOH) (2.94 mL, 1.46 mmol) and $\text{HSCH}_2\text{CH}_2\text{OH}$ (0.1 mL, 1.46 mmol) in MeOH (20 mL) was refluxed for 4h under nitrogen. The reaction mixture was cooled, neutralized with glacial AcOH and evaporated to dryness under vacuum. The residue was purified by silica gel column chromatography (10 % $\text{MeOH}/\text{CHCl}_3$) to afford 337 (74 mg, 80 %) as a white solid. 337: UV (H_2O) ϵ_{max} λ_{max} 247 nm ~~(ϵ 12,400)~~ (ϵ 12,400) (pH 2), 247.5 nm ~~(ϵ 13,000)~~ (ϵ 13,000) (pH 7), 253 nm ~~(ϵ 13,100)~~ (ϵ 13,100) (pH 11). Anal. ($\text{C}_{10}\text{H}_9\text{FN}_4\text{O}_3 \cdot 0.2\text{H}_2\text{O}$) C, H, N.

Please replace the paragraph starting at page 88, line 10 with the following amended paragraph:

~~9-(2,3-dideoxy-2-fluoro- β -L-glycero-pent-2-enofuranosyl)hypoxanthine~~

9-(2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl)hypoxanthine (338). A mixture of 330 (100 mg, 0.369), NaOMe (0.5 M solution in MeOH) (2.94 mL, 1.46 mmol) and $\text{HSCH}_2\text{CH}_2\text{OH}$ (0.1 mL,

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1.46 mmol) in MeOH (20 mL) was refluxed for 4h under nitrogen. The reaction mixture was cooled, neutralized with glacial AcOH and evaporated to dryness under vacuum. The residue was purified by silica gel column chromatography (10 % MeOH/CHCl₃) to afford 338 (70 mg, 80 %) as a white solid. 338: UV (H₂O) ϵ_{\max} λ_{\max} 247.5 nm (ϵ 12,700) (pH 2), 247.5 nm (ϵ 13,700) (pH 7), 252.5 nm (ϵ 13,100) (pH 11). Anal. (C₁₀H₉FN₄O₃ .0.3H₂O) C, H, N.

Please replace the paragraph starting at page 88, line 18 with the following amended paragraph:

~~2-Fluoro-6-amino-9-(2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl)purine~~

2-Fluoro-6-amino-9-(2,3-dideoxy-2-fluoro- β -L-glycero-pent-2-enofuranosyl)purine (339). A

solution of 31 (101 mg, 0.26 mmol) in dry acetonitrile (15 mL) was treated with TBAF (1 M solution in THF) (0.35 mL, 0.35 mmol) and stirred for 30 min. After evaporation of solvent, the dryness was purified by column chromatography (9 % CH₂Cl₂/MeOH) to obtain 339 (64.7 mg, 0.24 mmol, 92.3 %) as a white crystalline solid. UV (H₂O) ϵ_{\max} λ_{\max} 269.0 nm (pH 7).

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Please replace the paragraph starting at page 89, line 1 with the following amended paragraph:

~~2-Fluoro-6-amino-9-(2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl)purine~~

2-Fluoro-6-amino-9-(2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl)purine (340). A

solution of 333 (73.4 mg, 0.19 mmol) in dry acetonitrile (10 mL) was treated with TBAF (1 M solution in THF) (0.25 mL, 0.25 mmol) and stirred for 30 min. After evaporation of solvent, the dryness was purified by column chromatography (9 % CH₂Cl₂/MeOH) to obtain 340 (46.2 mg, 0.17 mmol, 90.3 %) as a white crystalline solid. UV (H₂O) ϵ_{\max} λ_{\max} 269.0 nm (pH 7).

Please replace the paragraph starting at page 89, line 6 with the following amended paragraph:

~~2-Amino-6-chloro-9-(2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl)purine~~

2-Amino-6-chloro-9-(2,3-dideoxy-2-fluoro- β -L-glycero-pent-2-enofuranosyl)purine (341). A

solution of 332 (143.5 mg, 0.40 mmol) in dry acetonitrile (15 mL) was treated with TBAF (1 M solution in THF) (0.6 mL, 0.60 mmol) and stirred for 30 min. After evaporation of solvent, the dryness was purified by column chromatography (5 % CH₂Cl₂/MeOH) to obtain 341 (109 mg, 0.382 mmol, 95.5 %) as a white crystalline solid. UV (H₂O) ϵ_{\max} λ_{\max} 308.5 nm (pH 7).

Please replace the paragraph starting at page 89, line 11 with the following amended paragraph:

~~2-Amino-6-chloro-9-(2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl)purine~~

2-Amino-6-chloro-9-(2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl)purine (342). A

solution of 334 (145 mg, 0.36 mmol) in dry acetonitrile (10 mL) was treated with TBAF (1 M solution in THF) (0.5 mL, 0.50 mmol) and stirred for 30 min. After evaporation of solvent, the dryness was purified by column chromatography (9 % CH₂Cl₂/MeOH) to obtain 342 (99.9 mg, 0.35 mmol, 96.4 %) as a white crystalline solid. UV (H₂O) ϵ_{\max} λ_{\max} 309.0 nm (pH 7).

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Please replace the paragraph starting at page 89, line 16 with the following amended paragraph:

~~9-(2,3-dideoxy-2-fluoro- β -L-glycero-pent-2-enofuranosyl)guanine~~

9-(2,3-dideoxy-2-fluoro- β -L-glycero-pent-2-enofuranosyl)guanine (343). A mixture of **341** (63.6 mg, 0.223 mmol), 2-mercaptoethanol (0.06 mL, 0.89 mmol) and 1 N NaOMe (0.89 mL, 0.89 mmol) in MeOH (10 mL) was refluxed for 5 h under nitrogen. The mixture was cooled, neutralized with glacial AcOH and concentrated to dryness under reduced pressure. The residue was purified by column chromatography (12 % CH₂Cl₂/MeOH) to obtain **343** (30.1 mg, 0.113 mmol, 50.7 %) as a white solid. UV (H₂O) ϵ_{max} λ_{max} 253.5 nm (pH 7).

Please replace the paragraph starting at page 89, line 22 with the following amended paragraph:

~~9-(2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl)guanine~~

9-(2,3-dideoxy-2-fluoro- α -L-glycero-pent-2-enofuranosyl)guanine (344). A mixture of **342** (59.3 mg, 0.208 mmol), 2-mercaptoethanol (0.07 mL, 1.04 mmol) and 1 N NaOMe (1.04 mL, 1.04 mmol) in MeOH (10 mL) was refluxed for 5 h under nitrogen. The mixture was cooled, neutralized with glacial AcOH and concentrated to dryness under vacuum. The residue was purified by column chromatography (12.5 % CH₂Cl₂/MeOH) to obtain **344** (28.0 mg, 0.105 mmol, 50.5 %) as a white solid. UV (H₂O) ϵ_{max} λ_{max} 253.0 nm (pH 7).